SPIRO-BISHETEROCYCLIZATION OF 5-METHOXYCARBONYL-2,3-DIHYDRO-2,3-PYRROLEDIONES WHEN TREATED WITH ACTIVATED ENAMINES

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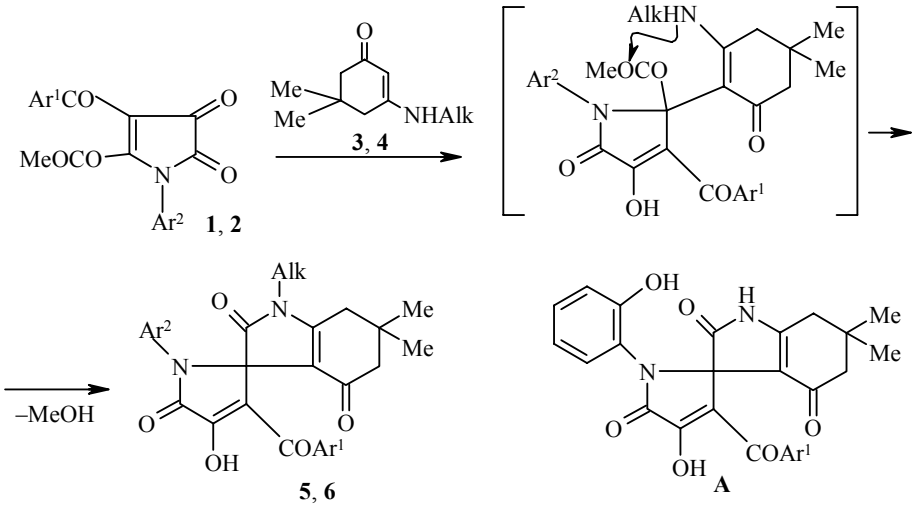
While continuing studies of recyclization and heterocyclization of 4-acyl-5-alkoxycarbonyl-1-aryl-2,3-dihydro-2,3-pyrrolediones when treated with binucleophilic reagents (*o*-aminophenol and N-phenyl-*o*-phenylenediamine [1], *o*-phenylenediamine [2], *o*-aminothiophenol [3], arylhydrazines [4, 5]), we studied a reaction that has been unknown for monocyclic 2,3-dihydro-2,3-pyrrolediones, the reaction of 1-aryl-4-aroyl-5-methoxycarbonyl-2,3-dihydro-2,3-pyrrolediones **1**, **2** with CH-, NH-binucleophiles: activated enamines (3-alkylamino-5,5-dimethyl-2-cyclohexen-1-ones **3, 4**).

When pyrrolediones **1, 2** are briefly refluxed (5-10 min) in absolute benzene with enamines **3, 4** (1:1), 1-alkyl-6,6-dimethyl-2,4-dioxo-2,3,4,5,6,7-hexahydro-1H-indole-3-spiro-2-(1-aryl-3-aroyl-4-hydroxy-5-oxo-2,5-dihydro-1H-pyrroles) **5, 6** are formed in practically quantitative yields. The spectral characteristics of compounds **5, 6** are quite close to those of model compounds **A**, the structure of which has been confirmed by X-ray diffraction data [6].



1, **5** Ar^1 = *p*-$O_2NC_6H_4$; **2**, **6** Ar^1 = Ph; **1**, **5** Ar^2 = Ph; **2**, **6** Ar^2 = *p*-ClC_6H_4; **3**, **5** Alk = CH_2Ph; **4**, **6** Alk = C_6H_{11}-*c*

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Probably in the first step of the reaction, addition of enamines **3, 4** occurs with participation of their activated β-CH group at the 5 position of pyrroledions **1, 2**, as described for reactions of these pyrrolediones with binucleophiles in [1-5], followed by intramolecular closure of the pyrrole ring due to nucleophilic attack by the alkylamino group on the ester carbonyl group and cleavage of methanol. The described reaction is a very rare example of regioselective assembly of the previously not very accessible spiro-bisheterocyclic system indole–spiro-pyrrole with goal-directed variable functional substituents in several positions of both heterocycles.

1-Benzyl-6,6-dimethyl-2,4-dioxo-2,3,4,5,6,7-hexahydro-1H-indole-3-spiro-2-(4-hydroxy-3-*p*-nitro-benzoyl-5-oxo-1-phenyl-2,5-dihydro-1H-pyrrole) (5). A solution of pyrroledione **1** [7] (5 mmol) and enamine (5 mmol) **3** in absolute benzene (2 ml) was refluxed for 10 min and then cooled down; after 24 hours, the precipitate was filtered out. Yield 95%; mp 254-256°C (with decomposition, from ethylacetate). IR spectrum (vaseline oil), ν, cm^{-1}: 3250 broad (OH), 1751, 1735 ($C_{(2)}=O_{indole}$, $C_{(5)}=O_{pyrrole}$), 1671, 1631 ($C_{(4)}=O_{indole}$, COPh). ^1H NMR spectrum (400 MHz, DMSO-d_6, HMDS), δ, ppm (*J*, Hz): 0.64 (3H, s, CH_3); 0.85 (3H, s, CH_3); 2.07, 2.12 (2H, two d, *J* = 16.2, $C_{(7)}H_2$); 2.18, 2.57 (2H, two d, *J* = 18.6, $C_{(5)}H_2$); 4.81, 4.95 (2H, two d, *J* = 16.5, $\underline{CH_2}$Ph); 6.95-7.45 (10H, group of multiplets, 2Ph); 7.86, 8.35 (4H, two d, *J* = 8.9,$C_6H_4NO_2$-*p*); 12.00 (1H, br. s, OH). Found, %: C 68.66; H 4.68; N 7.31. $C_{33}H_{27}N_3O_7$. Calculated, %: C 68.62; H 4.71; N 7.27.

1-Cyclohexyl-6,6-dimethyl-2,4-dioxo-2,3,4,5,6,7-hexahydro-1H-indole-3-spiro-2-(3-benzoyl-1-*p*-chlorophenyl-4-hydroxy-5-oxo-2,5-dihydro-1H-pyrrole) (6). Yield 95%; mp 251-252°C (with decomposition, from ethyl acetate). IR spectrum (vaseline oil), ν, cm^{-1}: 3210 broad (OH), 1745 ($C_{(2)}=O_{indole}$, $C_{(5)}=O_{pyrrole}$), 1660 broad ($C_{(4)}=O_{indole}$, COPh). ^1H NMR spectrum (400 MHz, DMSO-d_6, HMDS), δ, ppm: 0.63 (3H, s, CH_3); 0.87 (3H, s, CH_3); 1.34 (2H, m, $CH_{2cyclohexyl}$); 1.64 (2H, m, $CH_{2cyclohexyl}$); 1.81-2.05 (6H, m, $3CH_{2cyclohexyl}$); 1.94, 2.04 (2H, two d, *J* = 16.1, $C_{(7)}H_2$); 2.52, 2.60 (2H, two d, *J* = 18.1, $C_{(5)}H_2$); 3.75 (1H, m, CH); 7.00-7.65 (9H, group of multiplets, Ph+C_6H_4); 12.48 (1H, br. s, OH). Found, %: C 68.69; H 5.52; Cl 6.40; N 5.00. $C_{32}H_{31}ClN_2O_5$. Calculated, %: C 68.75; H 5.59; Cl 6.34; N 5.01.

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